## REMARKS/ARGUMENTS

Claims 1-33 are pending in the application. Claims 1 and 19 have been amended to include the method step of regenerating a transformed plant from said plant cell and to require that the pathogenicity of said fungus to said transformed plant is reduced in comparison to the pathogenicity of said fungus to a plant that has not been transformed. Support for the amendments is provided in the original claims and in the specification, for example, on page 10. No new matter has been added by way of amendment. Reexamination and reconsideration of the claims are respectfully requested.

### The Objection to Claim 19 Should Be Withdrawn

The Office Action (January 30, 2004, page 2) has objected to claim 19 as incorrectly referring to SEQ ID NO:10 in the alternative. The claim has been amended to correct the error. Accordingly, this objection to claim 19 has been obviated by amendment and should be withdrawn.

### The Rejection of Claims under 35 U.S.C. §112, Second Paragraph, Should Be Withdrawn

The Office Action (January 30, 2004, page 2) has rejected claims 1-4, 8, 19-22, and 29 under 35 U.S.C. §112, second paragraph, as being indefinite.

Claims 1 and 19 were deemed indefinite because the preamble lacked correlation with the last method step. These claims have been amended to add a step to the method as suggested; accordingly, this rejection has been obviated by amendment and should be withdrawn.

Claim 20 was rejected because "said plant cell" lacked antecedent basis. Claim 20 has been amended as indicated; accordingly, this rejection has been obviated by amendment and should be withdrawn.

The remaining claims specified in the rejection (claims 2-4, 8, 21-22, and 29) are either dependent on or incorporate the limitations of amended claims 1, 19, or 20 and therefore have also been amended to obviate this rejection. Accordingly, this rejection to the claims has been obviated and should be withdrawn.

The Rejection of Claims Under 35 U.S.C. §112, First Paragraph, Should Be Withdrawn

The Office Action (January 30, 2004, page 2 *et seq.*) has rejected claims 1-33 as failing to comply with the enablement requirement. Applicants respectfully traverse this rejection.

The Office Action states (page 4, first paragraph) as a basis for the enablement rejection that "the reaction catalyzed by microbial esterase or amine oxidase may be reversible, and might have therefore failed to protect plant cells from the fumonisin and/or AP1." Applicants respectfully disagree with this statement. If the Examiner is making this assertion on the basis of personal knowledge, Applicants respectfully request that the Examiner provide an affidavit under 37 C.F.R. §1.104(d)2 so that Applicants can properly evaluate the basis for the rejection. Applicants are submitting herewith a Rule 132 declaration of one of the inventors, Jon Duvick (see Appendix A). As stated in the declaration, the reactions mentioned are not likely to be reversible under normal pH levels and substrate concentrations.

The Office Action states (page 4, first paragraph) as a basis for the enablement rejection that "it is uncertain how the metabolism of the reaction products (for example, 2-OP and ammonia) might affect the plant.... It is also uncertain, even if fumonisin produced by an invading fungus was efficiently converted to a non-toxin form, whether this conversion would impart reduced fumonisin toxicity upon the plant." Applicants respectfully disagree with this statement. Applicants are submitting herewith a Rule 132 declaration of one of the inventors, Jon Duvick (see Appendix A). As stated in the declaration, the metabolic product 2-OP has been demonstrated to be nontoxic with respect to sphingolipid metabolism and has been shown to be nonmutagenic in a preliminary Ames test. Further, 2-OP shows no similarity to known toxins, so there is no reason to believe it would be toxic, and no reason to believe that it would adversely affect a plant.

The Office Action states (page 4, first paragraph) as a basis for the enablement rejection that "[i]t is also uncertain, even if fumonisin produced by an invading fungus was efficiently converted to a non-toxin form, whether this conversion would impart reduced fumonisin toxicity upon the plant." Applicants respectfully disagree with this statement. Applicants are submitting herewith a Rule 132 declaration of one of the inventors, Jon Duvick (see Appendix A). As stated in the declaration, the rationale for this statement in the Office Action is unclear, because

converting a compound to a non-toxic form would necessarily result in reducing the toxicity of that compound to a plant. In fact, the present specification provides working examples which demonstrate that the metabolism of fumonisin to AP1 resulted in at least a 30-fold decrease in toxicity to plant tissues and as much as a 100-fold decrease in toxicity to plant cells (see Example 3, page 36, and Example 4, page 37).

For the reasons discussed above, Applicants disagree with the rationales for the enablement rejection that are stated in the Office Action. Moreover, those of skill in the art are aware that the expression of detoxification enzymes in plants has been shown to confer resistance against pathogenic bacteria. For example, Lu *et al.* (1998) (Abstract 5.4.3, presented at 7th International Congress of Plant Pathology, 9-16 August 1998, Edinburgh, Scotland; Appendix B) reported that expression of the wheat oxalate oxidase gene in transgenic sunflower plants significantly enhanced resistance of the transgenic plants to the fungal pathogen *Sclerotinia*. Further, Zhang *et al.* (1999) (*Nature Biotechnology* 17: 1021-1024; Appendix C) reported that transgenic sugarcane that was transformed with an albicidin detoxifying gene from *Xanthomonas albilineans* exhibited a high level of resistance to leaf scald disease (see page 1021, abstract and col. I). Thus, those of skill in the art are aware that transgenic plants expressing detoxification genes exhibit increased disease resistance and that pathogenicity to such plants of pathogenic plant fungus is reduced.

In view of the above arguments and amendments, Applicants respectfully submit that all grounds for rejection under 35 U.S.C. § 112, first paragraph, have been overcome. Accordingly, the rejection of claims under 35 U.S.C. § 112, first paragraph, should be withdrawn.

The Office Action (January 30, 2004, page 5) has rejected claims 1-33 for failing to meet the written description requirement. The Office Action (page 5) states that:

> The claimed invention does not meet the current written description requirements because SEQ ID NO: 16 and SEQ ID NO: 18 are partial DNAs encoding partial proteins. The claims encompass any full-length genes, fusion constructs and cDNAs comprising SEQ ID NO: 16 or 18. The disclosed structural feature does not necessarily constitute a substantial portion of the claims genus.

(emphasis in original) Applicants respectfully traverse this rejection.

In the Amendment filed November 27, 2002, Applicants added new sequences to the sequence listing at the request of the Examiner. These new sequences include SEQ ID NO: 16, which is the same as SEQ ID NO: 5 from U.S. Pat. No. 6,211,435, and SEQ ID NO: 18, which is the same as SEQ ID NO: 10 from U.S. Pat. No. 6,211,435. SEQ ID NO: 16 encodes SEQ ID NO: 17 (which is the same as SEQ ID NO: 6 from U.S. Pat. No. 6,211,435) and SEQ ID NO: 18 encodes SEQ ID NO: 19 (which is the same as SEQ ID NO: 11 from U.S. Pat. No. 6,211,435). As discussed in the specification, particularly for example on pages 9 and 11, the enzymes and nucleotide sequences of the present invention provide a means for additional catabolism of the fumonisin-degradation products obtained from degradation with other enzymes, such as, for example, these amino polyolamine oxidase (APAO) enzymes previously described in U.S. Patent No. 6,211,435. Other amine oxidase enzymes are known in the art.

As explained in U.S. Pat. No. 6,211,435 (see, *e.g.*, col. 2, lines 64-67), the sequence set forth as SEQ ID NO: 16 of the present application encodes "trAPAO," a truncated but still functional APAO enzyme. This trAPAO is "capable of oxidatively deaminating the AP1 to a compound identified as the 2-oxo derivative of AP1 or its cyclic ketal form (abbreviated as 2-OP….)" The sequence set forth as SEQ ID NO: 18 of the present application contains the nucleotide sequence of trAPAO with an additional lysine (see, *e.g.*, col. 3, lines 38-39 of U.S. Pat. No. 6,211,435). Thus, while the trAPAO sequences set forth in SEQ ID NOs: 16 and 18 of the present application are shorter than the full-length, native APAO sequences, they encode proteins having amine oxidase activity. SEQ ID NO: 16 is 1389 nucleotides long, and SEQ ID NO: 18 is 1392 nucleotides long.

The Office Action concludes that "[t]he claimed invention does not meet the current written description requirements because SEQ ID NO: 16 and SEQ ID NO: 18 are partial DNAs encoding partial proteins." Applicants respectfully disagree with this conclusion.

Claims 1-9, 19, 21-22, and 29 are method claims. Independent claim 1 is drawn to a method of reducing pathogenicity to a plant of a fungus that produces fumonisin, comprising stably integrating into the genome of a plant cell a first nucleotide sequence that has at least 95% sequence identity to the sequence set forth in SEQ ID NO: 16, 18, 20, 22, 24, 26, 28, 30, or 32 and encodes a

polypeptide having amine oxidase activity; optionally stably integrating into the genome of said plant cell a second nucleotide sequence that has at least 95% sequence identity to the sequence set forth in SEQ ID NO: 12 or 14 and encodes a polypeptide having fumonisin esterase activity; stably integrating into the genome of said plant cell a nucleotide sequence that has at least 95% sequence identity to the sequence set forth in SEQ ID NO: 2, 4, 7, or 10 and encodes a polypeptide having fumonisin detoxification activity; and regenerating a transformed plant from said plant cell, whereby the pathogenicity of said fungus to said transformed plant is reduced in comparison to the pathogenicity of said fungus to a plant that has not been transformed. Claims 2-9, 21-22, and 29 are dependent on claim 1 or incorporate the limitations of claim 1.

Independent claim 19 is drawn to a method of reducing pathogenicity to a plant of a fungus that produces fumonisin, comprising stably integrating into the genome of a plant cell a first nucleotide sequence that encodes a polypeptide having at least 95% sequence identity to the sequence set forth in SEQ ID NO: 17, 19, 21, 23, 25, 27, 29, 31, or 33 and has amine oxidase activity; optionally stably integrating into the genome of said plant cell a second nucleotide sequence that encodes a polypeptide having at least 95% sequence identity to the sequence set forth in SEQ ID NO: 13 or 15 and has fumonisin esterase activity; stably integrating into the genome of said plant cell a nucleotide sequence that encodes a polypeptide having at least 95% sequence identity to the sequence set forth in SEQ ID NO: 3, 5, 8, or 11 and has fumonisin detoxification activity; and regenerating a transformed plant from said plant cell, whereby the pathogenicity of said fungus to said transformed plant is reduced in comparison to the pathogenicity of said fungus to a plant that has not been transformed.

Independent claims 10 and 18 are composition claims with sequence limitations similar to those in claim 1. Claims 11-17, 24-25, and 32 are dependent on or incorporate the limitations of claim 10, and claims 23, 26-28, 30, 31, and 33 are dependent on claim 18. Thus, all of the claims specify either: a nucleotide sequence that has at least 95% sequence identity to the sequence set forth in SEQ ID NO: 16, 18, 20, 22, 24, 26, 28, 30, or 32 and encodes a polypeptide having amine oxidase activity; or a nucleotide sequence that encodes a polypeptide that has at least 95% sequence identity to the sequence set forth in SEQ ID NO: 17, 19, 21, 23, 25, 27, 29, 31, or 33 and also has amine oxidase activity.

The Office Action (page 5) concludes that "Applicant has not described a representative number of nucleotide sequences comprising SEQ ID NO: 16 or 18...." However, the recitation of at least 95% sequence identity is a *very predictable structure* of the sequences encompassed by the claimed invention. Applicants note that the description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. 66 Fed. Reg. 1099, 1106 (2001). Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. 66 Fed. Reg. 1099, 1106 (2001). Applicants submit that the knowledge and level of skill in the art would allow a person of ordinary skill to envision the claimed invention, *i.e.*, a nucleotide sequence that has at least 95% sequence identity to the sequence set forth in SEQ ID NO: 16, 18, 20, 22, 24, 26, 28, 30, or 32; or a nucleotide sequence that encodes a polypeptide having at least 95% sequence identity to the sequence set forth in SEQ ID NO: 17, 19, 21, 23, 25, 27, 29, 31, or 33.

Furthermore, the description of a claimed genus can be by structure, formula, chemical name, or physical properties. *See, Ex parte Maizel*, 27 USPQ2d 1662, 1669 (B.P.A.I. 1992), citing *Amgen v. Chugai*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). A genus of DNAs may therefore be described by means of a recitation of a representative number of DNAs defined by nucleotide sequence and falling within the scope of the genus, *or* by means of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *See*, *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1569 (Fed. Cir. 1997); *see also* Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, First Paragraph, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (2001). The recitation of a predictable structure of a nucleotide sequence that has at least 95% sequence identity to the sequence set forth in SEQ ID NO: 16, 18, 20, 22, 24, 26, 28, 30, or 32; or a nucleotide sequence that encodes a polypeptide having at least 95% sequence identity to the sequence set forth in SEQ ID NO: 17, 19, 21, 23, 25, 27, 29, 31, or 33 is sufficient to satisfy the written description requirement.

An Applicant, however, may also rely upon functional characteristics in the description, provided there is a correlation between the function and structure of the claimed invention. *See*

*Id.*, citing *Lilly* at 1568. All of the claims specify either: a nucleotide sequence that has at least 95% sequence identity to the sequence set forth in SEQ ID NO: 16, 18, 20, 22, 24, 26, 28, 30, or 32 and encodes a polypeptide having amine oxidase activity; or a nucleotide sequence that encodes a polypeptide having at least 95% sequence identity to the sequence set forth in SEQ ID NO: 17, 19, 21, 23, 25, 27, 29, 31, or 33 and also having amine oxidase activity. Thus, the claims recite functional characteristics of the claimed genus. Specifically, the claims recite that the sequences described with reference to SEQ ID NO: 16 or 18 further encode a polypeptide that has amine oxidase activity; thereby providing a functional characterization of the sequences claimed in the genus.

Example 14 of the "Synopsis of Application of Written Description Guidelines" is directed to a generic claim: a protein having at least 95% sequence identity to the sequence of SEQ ID NO:3, wherein the sequence catalyzes the reaction A → B. The synopsis materials conclude that the generic claim of Example 14 is sufficiently described under § 112, first paragraph, because: 1) "the single sequence disclosed in SEQ ID NO:3 is representative of the genus"; and 2) the claim recites a limitation requiring the compound to catalyze the reaction from A → B. The synopsis materials conclude that one of skill in the art would recognize that the Applicants were in possession of the necessary common attributes possessed by the members of the genus.

Following the analysis of Example 14, Applicants submit that the present claims satisfy the written description requirements of § 112, first paragraph. Specifically, the claims of the present invention encompass sequences having at least 95% sequence identity to the sequence set forth in SEQ ID NO: 16, 18, 20, 22, 24, 26, 28, 30, or 32 and encoding a polypeptide having amine oxidase activity; or a nucleotide sequence that encodes a polypeptide having at least 95% sequence identity to the sequence set forth in SEQ ID NO: 17, 19, 21, 23, 25, 27, 29, 31, or 33 and also having amine oxidase activity. As in Example 14, the specification discloses the nucleic acid sequences of SEQ ID NOs: 16 and 18 and the amino acid sequences of SEQ ID NOs: 17 and 19; in addition, the claims recite a limitation requiring the compound to have a specific function (*i.e.*, amine oxidase activity). Consequently, contrary to the conclusion stated in the Office Action, the sequences encompassed by the claims with reference to SEQ ID NOs: 16 and 18 are defined by

relevant identifying physical and chemical properties. The necessary common features of the claimed genus are clear.

Applicants further note that the Federal Circuit has explicitly stated that

> *Eli Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.

*Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1332 (Fed. Cir. 2003). *See also, Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1320 (Fed. Cir. 2003) (noting that "[i]n more recent cases, however, this court has distinguished *Lilly*" and further noting that in *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 323 F.3d 956 (Fed. Cir. 2002), "neither the specification nor the deposited biological material recited the precise 'structure, formula, chemical name, or physical properties' required by *Lilly*.")

In summary, the description of a representative number of species *does not* require the description to be of such specificity that it would provide individual support for each species that the genus embraces. Applicants submit that the relevant identifying physical and chemical properties of the disclosed genus would be clearly recognized by one of skill in the art and consequently, Applicants were in possession of the necessary common attributes or features of the elements possessed by the members of the genus. Accordingly, the rejection of claims 1-33 under 35 U.S.C. §112, first paragraph, for lack of written description should be withdrawn.

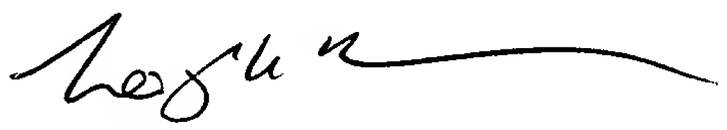
## CONCLUSION

In view of the above amendments and remarks, Applicants submit that the objections to the claims and the rejections of the claims under 35 U.S.C. §§112, first and second paragraphs, is overcome. Applicants respectfully submit that this application is now in condition for allowance. Early notice to this effect is solicited.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject Application, the Examiner is invited to call the undersigned.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,



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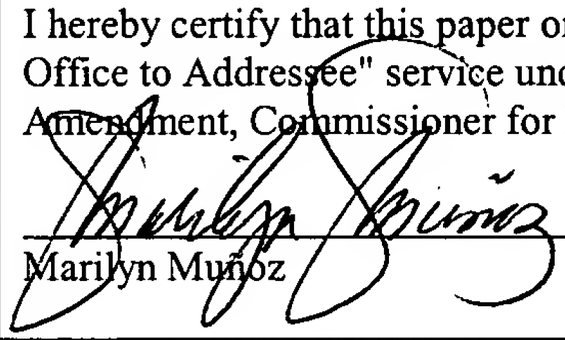

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